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Factors associated with adherence to glaucoma pharmacotherapy in the primary care setting

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Abstract

Background. Primary open-angle glaucoma is a leading cause of irreversible blindness.
Objectives. To identify factors associated with adherence to glaucoma pharmacotherapy in the primary care setting, focusing on physicians' role.
Methods. Patients were recruited from primary care clinics and telephone-interviewed using a structured questionnaire that addressed patient-, medication-, environment- and physicians-related factors. Patients' data on pharmacy claims were retrieved to calculate the medication possession ratio for measuring adherence.
Results. Seven hundred thirty-eight glaucoma patients were interviewed. The multivariate analysis identified eight variables that were associated independently with adherence. Barriers to adherence were found to be low income, believing that 'It makes no difference to my vision whether I take the drops or not' and relying on someone else for drop instillation (exp(B) = 1.91, $P = 0.002$; exp(B) = 2.61, $P < 0.0001$; exp(B) = 2.17, $P = 0.001$, respectively). Older age, having a glaucoma patient among close acquaintances, taking a higher number of drops per day, taking a prostaglandin drug and reporting that the ophthalmologist had discussed the importance of taking eye drops as prescribed, were found to promote adherence (exp(B) = 0.96, $P < 0.0001$; exp(B) = 0.54, $P = 0.014$; exp(B) = 0.81, $P = 0.001$; exp(B) = 0.37, $P < 0.0001$; exp(B) = 0.60, $P = 0.034$, respectively). No association was found between the patient's relationship with the family physician and adherence to glaucoma treatment.
Conclusion. Adherence to glaucoma pharmacotherapy is associated with patient-related, medication-related, physician-related and environmental factors. Ophthalmologists have a significant role in promoting adherence. However, the potential role of family physicians is unfulfilled and unrecognized.

Key words: Doctor–patient relationship, family physicians, glaucoma, patient adherence, primary care.

Introduction

Primary open-angle glaucoma (POAG), the most common type of glaucoma, is a leading cause of irreversible blindness, accounting for 2% of visual impairment and 8% of blindness globally (1). In 2011, 2.71 million persons in the USA had

POAG, with the highest estimated number among populations aged 70–79 years (2). In the UK, the National Health Service recently reported >1 million glaucoma-related visits per year (3). Early diagnosis and treatment of glaucoma has been found clinically beneficial and cost effective as it significantly delays visual field deterioration (4,5). Most patients receive intraocular pressure (IOP)-lowering topical medications for the treatment of glaucoma and need lifelong treatment and regular follow-ups to improve outcomes (6). Additionally, many glaucoma patients require more than one class of ocular hypotensive drugs to control their IOP (7). Whether measured by electronic monitoring (7), pharmacy claim data (8,9)or self-reporting (10), adherence to glaucoma pharmacotherapy, defined as the extent to which a patient follows a treatment plan as it was prescribed (11), is often poor (12).

Several studies have attempted to identify risk factors for non-adherence with glaucoma medications (8,9,13–15). Tsai and his colleagues suggested a systematic classification of barriers to adherence to glaucoma pharmacotherapy, grouped into four major areas: medical regimen, patient factors, situational or environmental factors and provider factors (13). The association between doctor–patient communication and adherence was highlighted by findings from the Glaucoma Adherence and Persistency Study (GAPS), which stressed the important role of the ophthalmologist (14). However, the role of the family physician in glaucoma care and specifically in promoting adherence to glaucoma pharmacotherapy has not yet been studied. It seems that the ophthalmologist and the family physician have different yet complementary roles in the care of glaucoma patients. The ophthalmologist is expected to make the diagnosis, provide explanations on the disease and its medical management, tailor the treatment regimen to the patient and conduct follow-up examinations. On the other hand, the family physician is well positioned to participate in the prevention and management of glaucoma, by ensuring that appropriate patients are screened for the disease, providing educational information about the disease and its treatment, detecting barriers to adherence to glaucoma pharmacotherapy and reinforcing good adherence and continuity of eye care (16). In health care systems where the family physician is the patient's case manager, the family physician provides monthly chronic prescriptions for all medical treatments, including ophthalmic medications. In spite of the important role family physicians might have in promoting adherence to glaucoma care among their patients, to our best knowledge, no study to date have explored whether family physicians actually fulfil this potential role. In addition, no study to date has explored the exact aspects of the communication with the ophthalmologist that are associated with better adherence.

This study aims to identify factors associated with adherence to glaucoma pharmacotherapy among patients with long-standing glaucoma in the primary care setting and to explore the role of the ophthalmologist and the family physician in this context.

Methods

Study design

A cross-sectional study was conducted in the Haifa and Western Galilee District of Clalit Health Services, Israel's largest government-funded Health Maintenance Organization, which has a well-established community care system and provides full medical coverage inclusive of pharmacy benefits for prescription medications to >50% of Israel's population and ~700 000 inhabitants of Haifa and its vicinity. A probability cluster sample was designed based first on randomly selecting primary care clinics and then choosing all eligible patients within those selected. According to the Clalit Health Services database, on 1 January 2008, 3457 eligible study candidates were registered in the 107 primary care clinics in Haifa and Western Galilee district. In view of the considerable variance in the rates of adherence to chronic pharmacotherapy raging from 75% to 37% (17,18), and the lack of prior data regarding the rates of adherence to IOP-lowering medications among patients with long-standing glaucoma in Israel, a sample size of 1070 patients was calculated, taking into account an estimated adherence rate of 50%, an estimated design effect (due to cluster sampling) of 1.8, accepting a two-sided significance level of 95% and a power of 80% and considering a possible non-response rate of 40%. To achieve this sample size, patients from 27 primary care clinics were included in the study and approached between November 2008 and May 2009.

Patients received a phone call from the study coordinator asking them to participate in the study. Upon their informed consent, participants underwent a 15-minute structured telephone interview in Hebrew or Russian according to their personal preference. Interviews were performed by four pre-trained interviewers, one of whom interviewed subjects in both Russian and Hebrew. Interviewers were blinded to information on interviewee's medication use behaviour in order to minimize bias. Retrospective data on prescription filling were retrieved from the Clalit Health Services database, which includes complete capture of medical, pharmacy and health care provider encounters of its members.

Study participants

The target population were patients with long-standing glaucoma who use multidrug glaucoma pharmacotherapy. Patients were considered for the study according to the following inclusion criteria: (i) documentation of glaucoma condition dated before 1 January 2000 in the Clalit Health Services computerised

database; (ii) aged ≥ 40 years and (iii) patient had been prescribed at least two different prescriptions for IOP-lowering topical medications during the study period (between 1 January and 31 December 2007). No selection by specific diagnosis of glaucoma was done because POAG is the most prevalent type in the elderly patient population (3). Patients who did not respond to three phone calls made on different days, and patients with hearing difficulties or language barriers who were not able to answer the phone interview conducted in Hebrew or Russian were excluded from the study.

Study questionnaire

A structured questionnaire was designed, based on the work of Tsai and his colleagues (13). The questionnaire includes 41 items, of which 30 items use a 1 (a lot) to 4 (not at all) Likert scale. It explores four domains as follows: patient-related factors (12 items); situational/environmental factors (three items); medication- related factors (17 items) and physician -related factors (nine items).

The questionnaire also includes items asking about sociodemographic characteristics: gender, date and country of birth, year of immigration to Israel, level of education, eligibility for copayment waiver (due to low socioeconomic status as defined by the Israel National Insurance Institute) and income (in comparison with 3700 NIS, ~1000 USD, the average net monthly income per standard person in Israel in 2006) (19). The questionnaire was constructed in Hebrew and was validated in the following manner: a multidisciplinary team, consisting of two board certified family physicians (OCC, KK), a board certified ophthalmologist (OG) and an epidemiologist (LKB), adapted the instrument to the study objectives. The wording of the questions was further piloted by administering the questionnaire to 10 glaucoma patients to ensure that the questions were intelligible and answerable. Patients were debriefed after completing the questionnaire, and the questionnaire was revised based on their comments. The questionnaire was first translated into Russian and then back translated into Hebrew, and the wording was changed accordingly to fit the correct meaning of each item.

Adherence measure

Data on pharmacy claims of study participants were used to measure adherence.

We used the medication possession ratio (MPR), a reliable measure of adherence in a closed pharmacy system (such as Clalit Health Services pharmacy system) (20), which has been applied before for measuring adherence to glaucoma medications (21). MPR is defined as the total days' supply of IOP-lowering topical medication divided by the number of participation days (i.e. the number of days between the first prescription fill during the study and the end of the study period). The study period for MPR calculations was defined between 1 January and 31 December 2007. The value of the days' supply was truncated if the supply extended beyond the study period. In combination therapy, the numerator was the sum of days' supply of all IOP-lowering topical medications, and the denominator was the sum of participation days for each drug in the regimen. In cases where an IOP-lowering medication was discontinued and replaced by a different medication containing a drug from the same class, the numbers of days' supply of the two medications were summed and the number of participation days was calculated from the day of the first prescription for the first medication till the end of the study period. However, in all other cases, it was impossible to verify whether prescriptions were not refilled because of non-adherence or due to medical decision (in such cases MPR would be falsely reduced).

Because the average number of drops per millilitre varies widely between different types of glaucoma medications (between 22 drops/ml to 42 drops/ml) (22), our calculations of the number of days of medication supply were based on previous studies that published the actual number of drops per bottle of medication (21,22). Bilateral eye drops were assumed for all patients: once daily use of prostaglandins and timolol gel-forming solutions; twice daily administration of beta-blockers, alpha-adrenergic agonists and carbonic anhydrase inhibitors and three administrations per day for pilocarpine. MPR was stratified into non-adherence for MPR < 0.8 and good adherence for MPR ≥ 0.8.

Statistical analysis

Descriptive statistics was used to describe participants' demographic and baseline characteristics and to assess overall adherence. Associations between dependent variable (MPR) and independent variables were assessed using *t*-test or chi-square analysis for continuous or categorical variables, respectively. Variables associated with adherence in the bivariate analyses ($P = 0.05$) were entered into a multivariate logistic regression model to seek the variables that best explain non-adherence. Demographic characteristics included in the model were gender, age and self-reported income. Both low level of education (i.e. ≤11 years of education) and eligibility for copayment waiver were closely associated with low self-reported income (i.e. reporting average monthly income < 3700 NIS; $P = 0.005$, $P < 0.0001$, respectively), and therefore were not included in the model. All analyses were performed using the SPSS version 18 statistical program (SPSS INC, Chicago, IL).

Results

Of the 1070 patients selected for interview, 332 (31%) were excluded. The main reasons for exclusion were not

responding after three telephone calls (20%), declining to participate in the study (8%) and denying having glaucoma or ever being treated with IOP-lowering medications (2%). The remaining 738 fulfilling the inclusion/exclusion criteria consented to participate in the study and constituted the study population. Of them, 513 subjects were interviewed in Hebrew and 225 (30%) in Russian. The multivariate analysis included 690 of 738 surveyed patients (93.5%) for whom complete survey data were available. On average, adherence to glaucoma pharmacotherapy among study participants was high (mean MPR = 1.1 ± 0.51) ranging from 0.11 to 3.81. Overall, 523 (71%) of study participants were classified as good adherents (MPR ≥ 0.8) and 215 (29%) as non-adherents (MPR < 0.8).

Table 1 presents study participants' sociodemographic and baseline characteristics. Good adherents and non-adherents differed in several characteristics. Compared with good adherents, non-adherents tended to be less educated (11 ± 4 years versus 12 ± 4 years of education, $P = 0.002$), have lower income (65% versus 53% declared earning an income below average, $P = 0.004$), use a smaller number of different types of IOP-lowering medications (31% versus 40% used three or more different types of medications, $P = 0.02$) and use less drops per day (3 ± 2 versus 4 ± 2 drops per day, $P < 0.0001$). Mean MPR was higher among patients who had a prostaglandin analogue included in their glaucoma medication regimen in comparison with patients who did not use this class of medication (mean MPR = 1.13 ± 0.49 versus 0.91 ± 0.55, $P < 0.0001$). There was no association between mean MPR and any other type of glaucoma medication included in the regimen ($P > 0.05$ for all, in unadjusted analyses).

Table 1. Demographic and baseline characteristics of study participants ($n = 738$)

Characteristic	
Age, years, mean (SD)	75.4 (9.7)
Gender, *n* (%)	
Female	418 (57)
Country of birth, *n* (%)	
Israel	106 (14)
Former Soviet Union	230 (31)
Asia/Africa	166 (23)
USA/Europe (excluding former Soviet Union)	236 (32)
Years since immigration to Israel (when applicable) mean (SD)	42 (19.6)
Years of education mean (SD)	11.5 (4)
Income, *n* (%)	
Below average	352 (48)
Eligible for copayment waiver, *n* (%)	282 (38)
No. of different IOP-lowering topical medications, mean (SD)	2.5 (0.8)
No. of drops per day, mean (SD)	3.6 (2.2)
IOP- lowering topical medication *n* (%)	
Alpha-agonist	253 (34)
Beta blocker	315 (43)
Carbonic anhydrase inhibitor	79 (11)
Miotics (pilocarpine)	83 (11)
Prostaglandin	629 (85)
Combination product	
Dorzolamide and timolol	414 (56)
Latanoprost and timolol	67 (9)

Patient-related factors, situational/environment-related factors and medication-related factors that were found to be associated with adherence to glaucoma pharmacotherapy in the bivariate analyses ($P < 0.05$) are presented in Table 2.

The association between physician-related factors and adherence to glaucoma pharmacotherapy is presented in Table 3. Having frequent appointments with a regular ophthalmologist who recommended IOP-lowering topical treatment and discussed the importance of adherence to treatment was associated with MPR ≥ 0.8 (i.e. good adherence), [relative risk (RR) = 1.13, $P = 0.04$; RR = 1.3, $P = 0.002$; RR = 1.47, $P = 0.01$, RR = 1.2, $P = 0.005$, respectively, all in unadjusted analyses]. Respondents who did not have a regular ophthalmologist, or were not satisfied with their relationship with him, also tended to believe that 'it makes no difference to my vision whether I take the drops or not' ($P = 0.002$; $P < 0.0001$, respectively, all in unadjusted analyses).

Although the majority of study participants (90%) described their relationship with the family physician as good, only 18% reported that the family physician ever discussed with them the importance of adherence to glaucoma treatment and even fewer (16%) claimed that their family physician had ever explained how to instil the eye drops (Table 3). However, respondents who did recall having a discussion with their family physician regarding the importance of adherence tended to believe less that "it makes no difference to my vision whether I take the drops or not" ($P = 0.03$). In addition, patients who rely on others to remind them to take the drops reported more often that the family physician had explained how to use the drops ($P = 0.04$).

As presented in Table 4, the multivariate analysis identified eight variables that were associated independently with adherence. Low income, believing that 'It makes no difference to my vision whether I take the drops or not' and relying on someone else for drop instillation were found to be barriers to adherence. Older age, having a glaucoma patient among relatives or close friends, taking a higher number of drops per day, taking a prostaglandin drug and reporting that the ophthalmologist discussed with the patient the importance of taking eye drops as prescribed were found to promote adherence. The multivariate model explained 19.8% of the variance (R^2).

Table 2. Patient-related, situational/environment-related, and medication-related factors associated with adherence to glaucoma pharmacotherapy (bivariate analyses)

Factors	Total, *n* (%)	Good adherence (MPR ≥ 0.8), *n* (%)	Non-adherence (MPR < 0.8), *n* (%)	*P* value
Patient-related factors—health status and disability				
Self-reported health status, *n* = 737				
Very good/good/reasonable	491 (67)	360 (69)	131 (61)	0.046
Not so good/bad	246 (33)	163 (31)	83 (39)	
Functional dependence in daily activities, *n* = 734				
Independent or needs help in cleaning or cooking	581 (79)	428 (82)	153 (73)	0.005
Needs help in ADL	153 (21)	95 (18)	58 (27)	
Having difficulty remembering to take the drops,[a] *n* = 713				
Yes	111 (16)	70 (14)	41 (21)	0.017
No	602 (84)	446 (86)	156 (79)	
Patient-related factors—attitudes and beliefs regarding glaucoma disease and treatment[a]				
Glaucoma is a serious disease, *n* = 707				
Yes	617 (87)	459 (89)	158 (82)	0.008
No	90 (13)	55 (11)	35 (18)	
Glaucoma can reduce my vision and make me blind, *n* = 704				
Yes	621 (88)	466 (91)	155 (82)	0.001
No	83 (12)	48 (9)	35 (18)	
I'm tired of taking the drops, *n* = 698				
Yes	235 (34)	155 (31)	80 (42)	0.004
No	463 (66)	353 (70)	110 (58)	
It makes no difference to my vision whether I take the drops or not, *n* = 698				
Yes	100 (14)	56 (11)	44 (23)	<0.0001
No	589 (86)	452 (89)	146 (77)	
I have a close friend or a relative who has had glaucoma, *n* = 701				
Yes	183 (26)	150 (29)	33 (17)	0.002
No	518 (74)	362 (71)	156 (83)	
Situational/environmental factors				
Someone else helps me with drop instillation, *n* = 714				
None	546 (77)	414 (80)	132 (67)	<0.0001
Family member or other caregiver	168 (23)	103 (20)	65(33)	
Someone else reminds to take glaucoma medications, *n* = 716				
None	590 (82)	439 (85)	151 (76)	0.004
Family member or other caregiver	126 (18)	78 (15)	48 (24)	
Medication-related factors—medication acquisition and drop instillation[a]				
It is difficult to reach the pharmacy for medication refill, *n* = 714				
Yes	233 (33)	155(30)	78 (39)	0.02
No	481 (67)	360 (70)	121 (61)	
It is difficult to open the bottle, *n* = 710				
Yes	82 (12)	51 (10)	31 (16)	0.028
No	628 (88)	463 (90)	165 (84)	
It is difficult to put drops in eyes, *n* = 709				
Yes	144 (20)	89 (17)	55 (28)	0.01
No	565 (80)	425 (83)	140 (72)	

ADL, activities of daily living.

[a]Yes: answered 1 or 2 and No: answered 3 or 4 on a 1–4 Likert scale (1 = agree a lot; 4 = don't agree).

Discussion

This study suggests that adherence to glaucoma pharmacotherapy is multifactorial and associated independently with factors related to all four domains explored.

Various risk factors were identified for patient non-adherence. Patients who depended on others with regard to their glaucoma pharmacotherapy were at greater risk for non-adherence, especially when living alone. Low income was found to be an

Table 3. The association between physician-related factors and adherence to glaucoma pharmacotherapy (bivariate analyses)

Factors	Total, *n* (%)	Good adherence (MPR ≥ 0.8), *n* (%)	Non-adherence (MPR < 0.8), *n* (%)	*P* value
Ophthalmologist-related factors[a]				
Regular ophthalmologist, *n* = 714				
Yes	643 (90)	472 (92)	171 (85)	0.002
No	71 (10)	40 (8)	31 (15)	
Scheduled appointment every 3 months, *n* = 715				
Yes	557 (78)	409 (80)	148 (73)	0.04
No	158 (22)	103 (20)	55 (27)	
Ophthalmologist recommended glaucoma topical treatment, *n* = 706				
Yes	682 (97)	500 (98)	182 (94)	0.01
No	24 (3)	12 (2)	12 (6)	
Ophthalmologist explained how to use the drops, *n* = 704				
Yes	630 (90)	464 (91)	166 (86)	0.06
No	74 (10)	47 (9)	27 (14)	
Ophthalmologist discussed the importance of taking drops as prescribed, *n* = 703				
Yes	575 (82)	430 (84)	145 (75)	0.005
No	128 (18)	80 (16)	48 (25)	
Having a good relationship with the ophthalmologist, *n* = 704				
Yes	611 (87)	451 (88)	160 (83)	0.06
No	93 (13)	60 (12)	33 (17)	
Family physician-related factors[a]				
Family physician explained how to use the drops, *n* = 703				
Yes	112 (16)	75 (15)	37 (19)	0.15
No	591 (84)	435 (85)	156 (81)	
Family physician discussed the importance of taking drops as prescribed, *n* = 701				
Yes	129 (18)	90 (18)	39 (20)	0.42
No	572 (82)	419 (82)	153 (80)	
Having good relationship with my family physician, *n* = 704				
Yes	636 (90)	465 (91)	171 (87)	0.34
No	68 (10)	46 (9)	22 (13)	

[a]Yes: answered 1 or 2 and No: answered 3 or 4 on a 1–4 Likert scale (1 = agree a lot; 4 = disagree).

independent barrier for adherence and was associated with low level of education, which in turn could result in difficulty in understanding the prescribed regimen and, thus, adhering to it (23). In addition, concerns about the threat of illness, the perceived burden of the disease and faith in treatment effectiveness were also important determinants of adherence. The belief that 'it makes no difference to my vision whether I take the drops or not' was found to be a substantial barrier to adherence to glaucoma medications and was significantly associated with other non-adherence characteristics, such as low self-reported health status.

According to our results, adherence improves with increasing age, as was previously reported (8), and with increased number of drop instillations per day. It was suggested that patients receiving higher dosing might have an advanced disease and receive more effective counselling from their physicians (8). We also found an association between better adherence and having a glaucoma patient among close acquaintances. This might also be due to better knowledge and understanding of the disease and its medical treatment. Using a prostaglandin medication was associated in our study with better adherence. Prostaglandins were associated in previous studies with better adherence than any other IOP-lowering medication, in both one-drug and two-drug regimens (7,9). Because our data are derived from pharmacy claims, we can only hypothesize as to the reasons for the better adherence with prostaglandins. As suggested previously by Nordstrom and her colleagues, this could be due to the once-a-day dosing of prostaglandins, fewer side effects and greater efficacy in lowering IOP, which would be associated with fewer changes of medications (9). This result stresses the role of the physician's choice of medication in promoting adherence to glaucoma pharmacotherapy. We found that physician–patient relations play an important role in patients' adherence to glaucoma pharmacotherapy. Other studies have also demonstrated that clinicians can influence patients' understanding and concerns about the threat of illness and the belief in the effectiveness of treatment, which are important determinants of adherence (17). According to our

Table 4. Logistic regression model for factors associated with non-adherence (MPR < 0.8) to glaucoma pharmacotherapy

Factors	Exp(B)	95% confidence interval		*p* value
		Lower	Upper	
Age [a]	0.96	0.94	0.98	<0.0001
Gender				
Female	Reference	0.65	1.46	0.90
Male	0.98			
Income				
Average and above	Reference	1.26	2.90	0.002
Below average	1.91			
Glaucoma patient among relatives or close friends				
No	Reference	0.33	0.88	0.014
Yes	0.54			
'It makes no difference to my vision whether I take the drops or not'				
No	Reference	1.56	4.35	<0.0001
Yes	2.61			
Someone else helps me with drop instillation				
No	Reference	1.36	3.47	0.001
Yes	2.17			
Number of drops per day[a]	0.81	0.73	0.9	<0.0001
Using a prostaglandin topical medication				
No	Reference	0.22	0.62	<0.0001
Yes	0.37			
Ophthalmologist discussed the importance of taking drops as prescribed				
No	Reference	0.36	0.96	0.034
Yes	0.60			

[a]Continuous variable.

results, merely explaining how to take the drops or having good relations in general with patients might not suffice to promote adherence. Only recalling a discussion with the ophthalmologist about the importance of taking the drops as prescribed was independently associated with better adherence. However, it is possible that patients with better adherence had a better recollection of the ophthalmologist's discussion with them, simply because taking the drops according to the doctor's instructions was already important to them.

Although in this study family physicians in general were not involved in glaucoma care, they provided an explanation regarding glaucoma treatment to patients who were at risk for non-adherence. Another clue for the potential role of the family physician was demonstrated by the finding that patients, who did recall a discussion with their family physician about the importance of adherence to glaucoma medications, had more faith in treatment effectiveness.

Refilled prescriptions at <80% of theoretically perfect adherence (100%) is an acceptable measure of non-adherence in glaucoma and other chronic conditions (18,24). About 29% of study participants were non-adherents to glaucoma pharmacotherapy (MPR < 0.8). Similar rates of non-adherence have been reported previously (12). Mean MPR in this study was >1.0, which can occur if patients use more than the prescribed amount of drops per dose, use more than the prescribed amount of doses per day, stockpile medication or lose a bottle or need to change their drug regimen. Additionally, the number of treatment days in an eye drop bottle may vary between different types of medications. For this reason, patients with more than one glaucoma medication might refill all their glaucoma prescriptions when they run out of one medication, even if they still have some of the adjunctive medications left. These behaviours may introduce some inaccuracy into the use of MPR as a measure of adherence to medication use. Other studies that explored adherence to chronic medical treatments were also challenged with over-adherence, ranging in one study form 12% (patients with gout) to 27% (patients with seizure disorder) (18). However, the logistics of using and monitoring the dosage of liquid medications are much more complex than the use of oral medications (such as capsules or tablets), which may lead to the higher rates of over-adherence found in this study (57.5%). One way of dealing with MPRs > 1 is to truncate MPR > 1 to 1 (18). In our study, all MPRs > 1 were included in the 'good adherence' group (MPR ≥ 0.8), making truncation unnecessary.

The MPR allows the incorporation of all medication used by each patient into one continuous number that enabled us to compare adherence between patients who are prescribed

multiple drugs (14,18,21). However, adherence is a multifaceted health behaviour that should be measured by multiple methods over longer periods in order to capture different elements of medication use.

Our data reflect the perceptions of experienced glaucoma patients who use multidrug glaucoma pharmacotherapy. Indeed, results might not be as sensitive to factors that influence adherence early in the course of treatment.

This study is one of the largest studies on the topic of adherence to glaucoma medications reported to date. Overall, study results are consistent with the literature, which allows the generalizability of the findings to other countries and health care systems. Our results also conform to the results of the GAPS, mainly in regard to the influence of doctor–patient communication on patients' adherence behaviour. Similarly to our results, the multivariate model of the GAPS explained 21% of the variance (14).

Finally, this study is the first one, to our knowledge, to examine the role of the family physician in promoting adherence to glaucoma pharmacotherapy.

Based on the results of this study, we can conclude that physicians whether ophthalmologists or family physicians can influence and even remediate some of the barriers to adherence to glaucoma pharmacotherapy, especially those related to patients' knowledge and attitudes. According to our results, physicians should discuss with each and every glaucoma patient the importance of taking the drops as prescribed, paying special attention to younger patients on less intensive drop regimens; they should also actively involve family members or other caregivers in this discussion, especially when the patient depends on someone else to instil the drops and, finally, they should include a prostaglandin in the glaucoma medication regimen whenever possible.

Further studies are needed to examine family physicians' attitudes regarding their role in glaucoma care. There is a room for intervention to enhance both ophthalmologists and family physicians ability to identify patients at risk for non-adherence and to promote their adherence-related consultation skills.

Declaration

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References

1. WHO. *Global Data on Visual Impairments 2010*. http://www.who.int/blindness/GLOBALDATAFINALforweb.pdf (accessed on 25 April 2014).
2. Vajaranant TS, Wu S, Torres M, Varma R. The changing face of primary open-angle glaucoma in the United States: demographic and geographic changes from 2011 to 2050. *Am J Ophthalmol* 2012; **154**: 303–314.e3.
3. King A, Azuara-Blanco A, Tuulonen A. Glaucoma. *BMJ* 2013; **346**: f3518.
4. Maier PC, Funk J, Schwarzer G, Antes G, Falck-Ytter YT. Treatment of ocular hypertension and open angle glaucoma: meta-analysis of randomised controlled trials. *BMJ* 2005; **331**: 134.
5. Tuulonen A. Cost-effectiveness of screening for open angle glaucoma in developed countries. *Indian J Ophthalmol* 2011; **59**: S24–30.
6. American Academy of Ophthalmology Glaucoma Panel. *Preferred Practice Pattern Guidelines. Primary Open-Angle Glaucoma*. San Francisco, CA: American Academy of Ophthalmology, 2010. http://one.aao.org/preferred-practice-pattern/primary-openangle-glaucoma-ppp--october-2010 (accessed on 27 May 2014).
7. Robin AL, Novack GD, Covert DW, Crockett RS, Marcic TS. Adherence in glaucoma: objective measurements of once-daily and adjunctive medication use. *Am J Ophthalmol* 2007; **144**: 533–40.
8. Gurwitz JH, Glynn RJ, Monane M *et al*. Treatment for glaucoma: adherence by the elderly. *Am J Public Health* 1993; **83**: 711–6.
9. Nordstrom BL, Friedman DS, Mozaffari E, Quigley HA, Walker AM. Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol* 2005; **140**: 598–606.
10. Kass MA, Meltzer DW, Gordon M, Cooper D, Goldberg J. Compliance with topical pilocarpine treatment. *Am J Ophthalmol* 1986; **101**: 515–23.
11. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005; **353**: 487–97.
12. Schwartz GF. Compliance and persistency in glaucoma follow-up treatment. *Curr Opin Ophthalmol* 2005; **16**: 114–21.
13. Tsai JC, McClure CA, Ramos SE, Schlundt DG, Pichert JW. Compliance barriers in glaucoma: a systematic classification. *J Glaucoma* 2003; **12**: 393–8.
14. Friedman DS, Hahn SR, Gelb L, *et al*. Doctor-patient communication, health-related beliefs, and adherence in glaucoma results from the Glaucoma Adherence and Persistency Study. *Ophthalmology* 2008; **115**: 1320–7, e1–3.
15. Rees G, Leong O, Crowston JG, Lamoureux EL. Intentional and unintentional nonadherence to ocular hypotensive treatment in patients with glaucoma. *Ophthalmology* 2010; **117**: 903–8.
16. Rowe S, MacLean CH, Shekelle PG. Preventing visual loss from chronic eye disease in primary care: scientific review. *JAMA* 2004; **291**: 1487–95.
17. DiMatteo MR, Haskard KB, Williams SL. Health beliefs, disease severity, and patient adherence: a meta-analysis. *Med Care* 2007; **45**: 521–8.
18. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy* 2008; **28**: 437–43.
19. Israel Central Bureau of Statistics. *Statistical Abstract of Israel 2008*. http://www1.cbs.gov.il/reader/shnaton/templ_shnaton.html?num_tab=st05_30&CYear=2008 (accessed on 25 April 2014).
20. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. *Ann Pharmacother* 2006; **40**: 1280–88.

21. Friedman DS, Quigley HA, Gelb L *et al*. Using pharmacy claims data to study adherence to glaucoma medications: methodology and findings of the Glaucoma Adherence and Persistency Study (GAPS). *Invest Ophthalmol Vis Sci* 2007; **48**: 5052–7.
22. Rylander NR, Vold SD. Cost analysis of glaucoma medications. *Am J Ophthalmol* 2008; **145**: 106–13.
23. Juzych MS, Randhawa S, Shukairy A, Kaushal P, Gupta A, Shalauta N. Functional health literacy in patients with glaucoma in urban settings. *Arch Ophthalmol* 2008; **126**: 718–24.
24. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. *Curr Med Res Opin* 2009; **25**: 2303–10.